

DECLARATION 2

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under § 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the subject application or any patent issued thereon.

This Declaration is being made in order to overcome the claim rejection according to 35 USC § 112.

The Examiner objects that the Applicant "has not shown any ability of the composition to lessen, much less prevent adhesion of the wound covering to the wound" and "has most definitely not shown how one of skill in the art would use this invention to prevent wound adhesion".

On the basis of our experimental results we have found out that the wound treated by the mixture of hyaluronate with potassium triiodide maintains a significantly greater amount of hyaluronate and said hyaluronate has a higher molecular weight compared to the hyaluronate present in the wound treated by hyaluronate alone. The experiment conditions were as follows: A shaved space on the back side of rats was cleaned by the distilled water and by the disinfectant AHD 2000. An excisional square wound was made by a scalpel and scissors. One of the following: a physiological solution, a solution of iodine complex (the same final concentration as in our preparation Hyiodine, containing hyaluronic acid with potassium triiodide), sodium hyaluronate (the same final concentration as in our preparation Hyiodine) and the mixture of hyaluronate with iodine complex (Hyiodine) was applied in 1 ml dose. In case of a round wound, a ring having the diameter of 2 cm was quilted in the round wound. All wounds were covered by a sterile gauze and the square ones were covered by elastic bandages in addition. The process of wound preparation is documented on figs. 2 a-d (Enclosure X). The surface of the wound was evaluated in selected time intervals. The quantification of the hyaluronate that remained within the wound was very difficult as the hyaluronate layer had to be scraped off without taking the granulation tissue which is extremely soft along. The results thus obtained were quite dispersed. However, visually it was clear that the wound that was treated by the mixture of hyaluronate with potassium triiodide contained more hyaluronate than the wound that was treated by hyaluronate alone. In a clinical investigation we have found out that the bandage that was applied together with the mixture of hyaluronate with potassium triiodide could be kept on the wound for 60 hours without adhering to the wound. In case of the application of hyaluronate alone (without potassium triiodide) some of the bandages started to adhere after 24 hours already and practically all of them were stuck to the wound within 48 hours. Moreover, we have measured the molecular weight of the hyaluronate in the wound. It is known that hyaluronate having a higher molecular weight has a greater ability to retain water and thus prevent the adhesion. It was proved that after the application of the mixture of hyaluronate with potassium triiodide, the molecular weight of hyaluronate decreased significantly more slowly than in case of the application of the hyaluronate only. The graph 3 (Enclosure XI) shows that the hyaluronate that was not applied in the mixture with potassium triiodide almost disappeared from the wound within 30 hours (its molecular weight was very strongly reduced). Therefore, the conclusion is that the hyaluronate in a combination with potassium triiodide according to the invention persists on the wound surface much longer than the hyaluronate alone (the hyaluronate molecular weight when in combination with potassium triiodide decreases much

more slowly than the one of the hyaluronate alone) and that is why the wound surface is moist for a longer time. This provides for a suitable environment for moist healing, prevents the sticking of the bandage to the wound and also the hyaluronate persisting on the wound surface increases the concentration of some healing factors within the wound. The main subject-matter of the invention lies in a preparation which provides for an ideal environment needed for the formation of the granulation tissue and other regeneration processes in the wound and prevents the adhesion of the bandage to the wound.

Regarding the objection that the Applicant has not shown how one of skill in the art would use this invention to prevent wound adhesion, please note [0013] and [0014] of US 2005/0181025 A1 which explicitly state the method of applying the composition. The paragraph [0013] mentions a direct or indirect application of the composition, while the indirect application is explained as an application "on a wound-contacting portion of a bandage". The paragraph [0014] further discloses that "A hyaluronic acid, iodine and potassium iodine composition is provided to a wound and covered, or the composition is applied to the wound covering, which is then applied to the wound". The results of the tests performed in order to examine the adhesion of the bandage to the wound were already mentioned above.

Figure 2a



Figure 2b

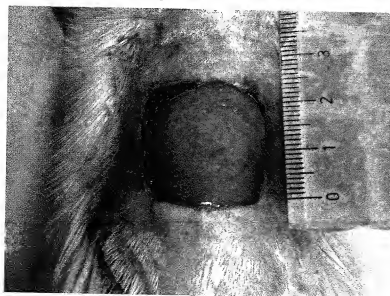
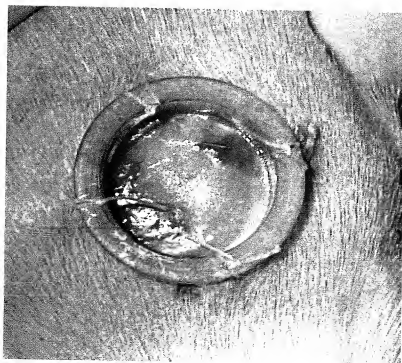


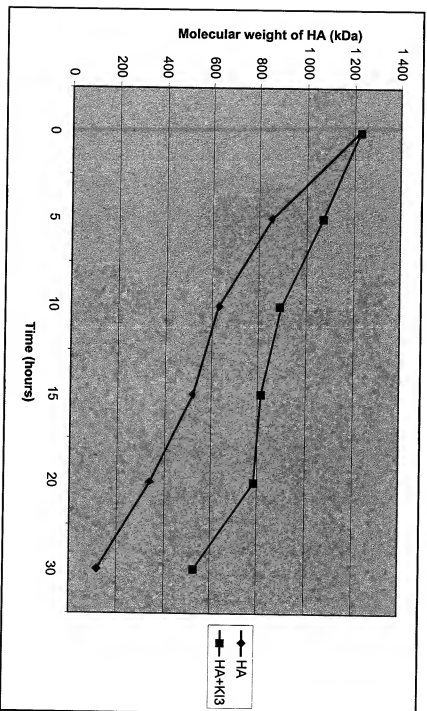
Figure 2c



Figure 2d



Graph 3



HA = hyaluronic acid;
HA+KI3 = the mixture of hyaluronic acid with potassium triiodide complex